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Heat and Cold Wave–Related Mortality Risk among United States Veterans with Chronic Obstructive Pulmonary Disease: A Case-Crossover Study

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Background: Chronic obstructive pulmonary disease (COPD) is a heterogeneous pulmonary disease affecting 16 million Americans. Individuals with COPD are susceptible to environmental disturbances including heat and cold waves that can exacerbate disease symptoms.

Objective: Our objective was to estimate heat and cold wave–associated mortality risks within a population diagnosed with a chronic respiratory disease.

Methods: We collected individual level data with geocoded residential addresses from the Veterans Health Administration on 377,545 deceased patients with COPD (2016 to 2021). A time stratified case-crossover study was designed to estimate the incidence rate ratios (IRR) of heat and cold wave mortality risks using conditional logistic regression models examining lagged effects up to 7 d. Attributable risks (AR) were calculated for the lag day with the strongest association for heat and cold waves, respectively. Effect modification by age, gender, race, and ethnicity was also explored.

Results: Heat waves had the strongest effect on all-cause mortality at lag day 0 [IRR: 1.04; 95% confidence interval (CI): 1.02, 1.06] with attenuated effects by lag day 1. The AR at lag day 0 was 651 (95% CI: 326, 975) per 100,000 veterans. The effect of cold waves steadily increased from lag day 2 and plateaued at lag day 4 (IRR: 1.04; 95% CI: 1.02, 1.07) with declining but still elevated effects over the remaining 7-d lag period. The AR at lag day 4 was 687 (95% CI: 344, 1,200) per 100,000 veterans. Differences in risk were also detected upon stratification by gender and race.

Discussion: Our study demonstrated harmful associations between heat and cold waves among a high-risk population of veterans with COPD using individual level health data. Future research should emphasize using individual level data to better estimate the associations between extreme weather events and health outcomes for high-risk populations with chronic medical conditions. https://doi.org/10.1289/EHP13176

Introduction

Anthropogenic climate change is causing harmful planetary effects with increased frequency, intensity, duration, and geographic extent of extreme weather events, including heat waves, droughts, wildfires, and floods.[1,2] Furthermore, climate change disproportionately affects children, the elderly, racial minorities, impoverished communities, and those living with underlying comorbidities such as chronic obstructive pulmonary disease (COPD).[1,3]

COPD is a heterogeneous, degenerative pulmonary disease characterized by airflow obstruction.[4] In the United States, $<6.2\%$ of adults had a diagnosis of COPD in 2017.[5] While the overall age adjusted mortality rates of COPD in the United States decreased in recent decades, improvements in COPD mortality were not equally distributed among the population. Age-adjusted mortality rates in males have decreased over time, but age-adjusted mortality rates in females remained relatively unchanged.[6,7] African American women were the only race-sex combination that had an increase in age-adjusted mortality rates from 2004 to 2018.[6] Individuals with COPD are often more susceptible to environmental perturbations due to compromised respiratory health and high rates of comorbidities, which lead to further debilitation and poorer health.[8,9]

While extremes in ambient temperature (heat and cold) are known to increase the risk of general mortality,[10–12] there is a dearth of evidence on heat and cold wave impacts at the individual level for populations with underlying chronic disease. Many studies evaluate the health risks from heat and cold waves using ecological time series analyses; however, these studies are limited in the ability to make inferences at the individual level, typically relying on aggregated counts of morbidity or mortality using hospital discharge or nonspecific government data. This complicates the development of public health interventions and impedes understanding of disease etiology by failing to assess individual level characteristics that may cause an individual to be more or less susceptible to extreme heat and cold. In addition, research findings based on the general population may not accurately represent the health risks experienced by those living with underlying chronic diseases who may be more susceptible to climate-related hazards.

To facilitate the development of improved public health interventions and climate change adaptation plans, we designed a time-stratified[13] case-crossover study[14] to examine the associations between heat and cold waves with all-cause mortality among a population of individuals diagnosed with COPD using data from the Veterans Health Administration (VHA) in the United States (2016 to 2021). We evaluated health disparities in heat and cold wave mortality risk for several effect modifiers: age, gender, race, and ethnicity.

Methods

Study Population

We extracted electronic health record data from the VHA Corporate Data Warehouse (CDW). The study population was derived from a source cohort of veterans[15] who had a diagnosis of COPD between 2016 to 2019 from the VHA ($N = 1{,}124{,}705$). We identified patients with COPD using at least two clinical encounters with an International Classification of Diseases Ninth Revision or Tenth Revision codes (ICD-9: 490, 491.XX, 492.XX, 496; or ICD-10: J40, J41.X, J42, J43.X, J44.X) for COPD (Table S1).[16] This included both veterans who were newly diagnosed or who had prevalent COPD between 2016 to 2019. We included patients

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>35 years of age and <100 years of age at the initial date of COPD diagnosis.

Our study included exposure information for only those veterans diagnosed with COPD who were deceased. Mortality data is updated quarterly by the VHA using data from the Social Security Master Death File, the Medicare Vital Status File, and the Veterans Benefits Administration's Beneficiary Identification and Records Locator System. Mortality events are only recognized if death certificates were made at a VHA facility or under their auspices or presented to the VHA by the National Cemetery Administration. This is done to protect veterans who are alive from being misclassified as deceased.[17]

Veterans living outside of the contiguous United States or who lived outside of the range of our weather data raster surface were excluded. Our outcome of interest was the association between heat and cold waves with all-cause mortality among this targeted veterans population with COPD. We obtained the following information from the VHA Patient Enrollee files in the CDW[17]: patients' age at death, self-reported gender (cisgender man, cisgender woman, transgender), self-reported race [American Indian/Alaska Native (AIAN), Asian American/Pacific Islander (AAPI), black, and white], self-reported ethnicity (Hispanic and non-Hispanic), and a geocoded residential address accurate up to 3 months prior to death. Race is a social construct to consider when evaluating the impacts systemic discrimination may have on exposure to climate-related hazards and subsequent health outcomes.

Environmental Data

We assigned daily meteorologic conditions (mean ambient temperature, total precipitation, mean specific humidity, and mean wind speed) to the residential addresses of the study cohort using data from GridMet.[18] GridMet is a blended dataset of Parameter elevation Regressions on Independent Slopes (PRISM) and the North American Land Data Assimilation System (NLDAS-2), obtained at a spatiotemporal resolution of daily 4- × 4-km grid cells.[18]

A 30-year distribution of weather data (1992 to 2021) was used to calculate percentile thresholds to determine heat and cold wave status. Using 30 years of meteorological data ensured we captured heat and cold waves that were anomalous for each veterans' geocoded residence in comparison to an historical record of usual weather conditions at their home location. We defined heat waves as two or more consecutive days whose mean ambient daily temperature was above the 90th percentile of warm season (April to September) mean ambient daily temperature values from 1992 to 2021 and cold waves as two or more consecutive days whose mean ambient daily temperature was below the 10th percentile of cold season (October to March) mean ambient daily temperature values from 1992 to 2021. The use of less extreme percentiles to define heat and cold waves is a newer concept in climate and health literature[19–23] but is important for a COPD study population that may be more susceptible to climate change and have a lower tolerance than the general population.

For the subset of veterans who lived near air monitors with valid data, daily mean fine particulate matter with aerodynamic diameter ≤2.5 μm ($PM_{2.5}$) concentrations were obtained from the United States Environmental Protection Agency (EPA)[24] air monitor networks from 1 December 2015 to the most recent available data at the time of our analysis, 11 November 2021. Air pollution is an important time-varying confounder of mortality that we could only assess in this subset population due to spatially incomplete monitor coverage. We removed outlying days exceeding the 99.5th and 0.5th $PM_{2.5}$ percentiles, as these may have been anomalies in the data recording process, and set any days with negative values for $PM_{2.5}$ to 0. Daily concentrations were assigned to the geocoded address of this subset population of veterans living within 10 km of an active $PM_{2.5}$ monitor by averaging all active $PM_{2.5}$ monitor values on a given day.

Study Design

We examined the associations between heat and cold waves with all-cause mortality using a time-stratified[13] case-crossover[14] study design. Each veteran's date of death was matched with referent days in the same year, month, and day of week as the date of mortality (event day), adjusting for confounding by season and day of week.[25] Under this matching strategy, each veteran was guaranteed at least 3 referent days. Since the case-crossover study design is a self-matched study, both observed and unobserved time-invariant confounding are controlled for by design, including unmeasured risk factors such as comorbidities, smoking history, genetics, or lifestyle.[26] We adjusted for daily time varying weather confounders, including precipitation, specific humidity, and wind speed. Specific humidity is a mass-based measurement of atmospheric moisture and is a better representation of suspended water vapor than relative humidity.[27] We also adjusted for holiday status, which included all federally recognized United States' holidays[28] and several other major holidays including Christmas Eve, New Year's Eve, Easter, and Halloween, as patients have different health seeking behaviors during holidays.

Statistical Analyses

Conditional logistic regression models were used to estimate incidence rate ratios (IRR)[26,29] describing associations between heat and cold wave exposure with all-cause mortality. Heat and cold wave assessments were restricted to warm (April to September) and cold (October to March) seasons, respectively. We examined delayed effects from lag day 0 to 7 (i.e., day of death to 7 d prior) where each lag was evaluated in a separate model.

Our statistical models assumed the following form:

$$\mathrm{logit}(\pi_{ik}) = \alpha_i + \beta_1 x_{ik1} + \beta_2 x_{ik2} + \beta_3 x_{ik3} + \beta_4 x_{ik4} + \beta_5 x_{ik5},$$

where β_1 is an indicator variable to denote heat or cold wave status for the ith person on the kth day of the matched set respectively, β_2 and β_3 are linear terms for precipitation and wind speed, β_4 is a linear term for specific humidity in the cold season model but is a natural cubic spline with 5 degrees of freedom for the warm season model, and β_5 is an indicator variable to denote holiday status. An assessment of nonlinearity among exposure variables identified heat wave status and specific humidity to have a nonlinear relationship. We used the Akaike information criterion (AIC) to determine an optimal parameterization to account for this nonlinear relationship, and a natural cubic spline with 5 degrees of freedom was chosen as the best smoother for specific humidity. No other nonlinear relationships were detected, and linear terms were deemed appropriate.

To test for effect modification and ascertain potential health disparities via societal discrimination and to measure biological effects of age on extreme weather susceptibility, we used stratified data subsets based on the effect modifiers of age at death, gender, race, and ethnicity. For age at death, we created a binary stratification for veterans <70 and ≥70 years of age. Models of heat and cold waves estimated IRRs for each subgroup. To determine the presence of effect modification, we employed a Z-test[30] to compare the IRRs of each strata at lag 0 to 7 d (Equation 1).

$$Z = (\beta_1 - \beta_2)/\mathrm{sqrt}\left((\mathrm{SE}_1)^2 + (\mathrm{SE}_2)^2\right) \tag{1}$$

Equation 1 is a Z-test formula to determine statistical significance of the difference between effect modifier estimates, where

β_1 and β_2 are the unexponentiated coefficients from the conditional logistic regression models for the two strata of effect modifiers being compared and SE_1 and SE_2 are their standard errors.

Missing data, which constituted a small proportion of our data, were treated as a separate stratum in our subgroup analyses and assumed missing at random. Attributable risks (AR) for the overall population were calculated for the strongest lag day (Equation 2).

$$AR = \frac{I_e}{p_e + \frac{1}{IRR - 1}} \quad (2)$$

Equation 2 is the attributable risk formula, where I_e is the season-specific mortality rate in the entire population of veterans with COPD, p_e is the proportion of control days that were exposed to heat or cold waves, and IRR is the effect estimate of heat and cold wave effects on mortality estimated via conditional logistic regression models.

All statistical analyses and maps were completed in R statistical software (version 4.1; R Development Core Team) within the secure Department of Veterans Affairs (VA) Informatics and Computing Infrastructure environment.

Sensitivity Analyses

We completed sensitivity analyses to examine model robustness against *a*) definitions of heat and cold waves (intensity, duration, and reference distribution), *b*) potential confounding from ambient air pollution, and *c*) the COVID-19 pandemic.

Multiple heat and cold wave definitions were evaluated. First, we reassigned heat and cold waves using alternative 95th, 97.5th, and 99th percentiles (heat waves) and 5th, 2.5th, and 1st percentiles (cold waves) of the 30-year mean temperature reference distribution during the warm and cold seasons to test model robustness to more severe heat and cold wave events. Second, we applied a shorter reference distribution of 20 years (2002 to 2021) to assess model sensitivity to recent patterns of climate exposure. Third, we excluded veterans who were exposed to heat or cold waves that lasted longer than 10 d and compared model results against our primary analysis. This was performed because under our primary definitions, some heat and cold wave events were anomalously long in duration. Fourth, we excluded veterans residing in areas with relatively mild 30-year percentile thresholds for both heat waves ($<25°C$) and cold waves ($>5°C$) and compared model results against our primary analysis. The purpose of this evaluation was to test the degree of influence veterans living in areas with mild climates had on the overall associations between heat and cold waves with all-cause mortality.

We assessed the potential role of air pollution, which could not be considered in our main models due to spatially incomplete air monitor data, in a subevaluation. We restricted our dataset to veterans living within a 10-km buffer of EPA $PM_{2.5}$ air monitors and ran separate models with and without adjustment for daily $PM_{2.5}$ as a confounder for both heat and cold wave events. Estimates for models with and without air pollution data were compared for the amount of confounding bias that may be present. Finally, since increased mortality likely occurred during the COVID-19 pandemic, we ran a stratified analysis comparing veterans who died pre and post 31 January 2020, the day the United States Department of Health and Human Services declared COVID-19 a public health emergency.[31] State level COVID-19 deaths at the weekly time interval were acquired from the National Center for Health Statistics[32] to be included as a time varying confounder if stratified analyses suggested differences in the heat and cold wave effect estimates pre and post the COVID-19 public health emergency declaration.

Ethics Statement

This study was approved by the institutional review boards at the Minneapolis VA and the University of Minnesota.

Results

Descriptive Statistics

The source cohort of veterans with COPD included 1,124,705 individuals. For our case-crossover study, we identified 377,545 deceased veterans with COPD. These deceased veterans lived in 3,058 out of 3,109 counties in the United States (98.4%). All 48 states and the District of Columbia were represented in the study sample (Figure 1). The study population was predominately male and older with the largest racial/ethnic group being non-Hispanic white (Table 1). All veterans identified died by December 2021.

Exposure to heat and cold waves in our study population occurred with 28.4% and 24.7% of patients having either an event or referent day exposed to heat waves and cold waves, respectively (Table 2). A total of 183,725 patients died during the warm season, resulting in a warm season mortality rate of 16,335 per 100,000 patients in this cohort of veterans with COPD. Of those who died during the warm season, 17,621 patients died during a heat wave event (9.6% of warm season mortality events). A total of 193,820 patients died during the cold season, resulting in a cold season mortality rate of 17,233 per 100,000 patients in the

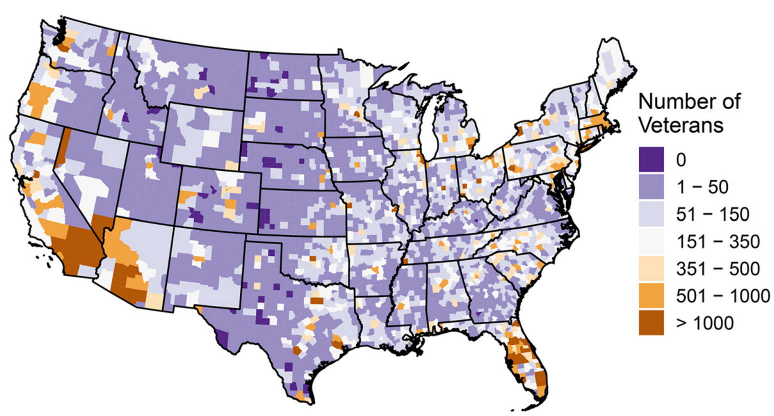

Figure 1. County level totals of deceased veterans with COPD (2016 to 2021, $n = 377{,}545$) in the VHA health care system based on county of residence at time of death. The map was created using R statistical software. Note: COPD, chronic obstructive pulmonary disease; VHA, Veterans Health Administration.

Table 1. Baseline characteristics of deceased veterans with COPD (2016 to 2021, $n = 377{,}545$) in the VHA health care system.

Characteristic	n (%)
Age at death [n (%)]	
<70 years	96,437 (25.6%)
70+ years	281,108 (74.4%)
Gender [n (%)]	
Cisgender male	369,535 (97.9%)
Cisgender female	8,004 (2.1%)
Transgender	6 (<1%)
Race [n (%)]	
White	298,978 (85.8%)
Black	42,754 (12.3%)
American Indian/Alaska Native	3,329 (<1%)
Asian American/Pacific Islander	3,600 (1%)
Missing[a]	28,884
Ethnicity [n (%)]	
Non-Hispanic	353,983 (97.8%)
Hispanic	7,889 (2.2%)
Missing	15,673

Note: Characteristics other than age at death were self-reported. COPD, chronic obstructive pulmonary disease; VHA, Veterans Health Administration.
[a]Missing data were not used in the calculation of percentages.

entire veteran population with COPD. Of those who died during the cold season, 13,961 patients died during a cold wave event (7.2% of cold season mortality events) (Table 2). The total number of study days (event and referent days) in the case crossover study classified as heat and cold waves were 9.4% and 7.1% of the total study period days within the warm and cold seasons, respectively (Table 2).

Table 3 demonstrates higher mean ambient temperatures during heat wave days on which patients died compared to non–heat wave days and lower mean ambient temperature during cold wave days on which patients died compared to non–cold wave days. Non–heat wave/non–cold wave days tended to have greater precipitation compared to heat wave days and cold wave days. Heat wave days tended to have greater atmospheric moisture than non–heat wave days, and the reverse was seen for cold waves (Table 3). For the subset of veterans living within 10 km of a valid $PM_{2.5}$ air monitor site ($n = 20{,}735$ warm season, $n = 21{,}535$ cold season), heat wave days had higher mean $PM_{2.5}$ concentrations than non–heat wave days (Table 3). Cold wave and non–cold wave days had similar $PM_{2.5}$ concentrations (Table 3). Similar trends in meteorological and air pollution levels were also observed for the referent days in our case-crossover dataset (Table S2).

Overall Associations

Associations between heat waves and all-cause mortality showed the strongest effect on lag day 0 with an IRR of 1.04 [95% confidence interval (CI): 1.02, 1.06]. Effects lasted until lag day 1 (IRR: 1.02; 95% CI: 1.00, 1.04) after which heat wave effects became attenuated (Figure 2). There was minimal effect of measured confounders (daily total precipitation, mean wind speed, mean specific humidity, and holiday status) on the heat wave effect estimate comparing crude and adjusted models (Table S3). Among patients exposed to heat waves on lag day 0, 651 (95% CI: 326, 975) deaths per 100,000 were attributable to heat waves. Cold waves increased the risk of all-cause mortality from lag days 2 to 7 with the strongest effect on lag day 4 with an IRR of 1.04 (95% CI: 1.02, 1.07). Effects of cold waves gradually increased from lag day 2, plateaued at lag day 4, and decreased through lag day 7 (Figure 2). A comparison of crude and adjusted cold wave models indicated potential confounding by measured confounders primarily on lag days 0 to 2, but minimal confounding of effect estimates from lag days 3 to 7 (Table S3). Among patients exposed to cold waves on lag day 4, 687 (95% CI: 344; 1,200) per 100,000 deaths were attributable to cold waves.

Stratified Analyses

We used stratified analyses to examine effect modification of heat and cold wave associations with all-cause mortality with respect to age, gender, race, and ethnicity.

Age. Heat waves increased the risk of all-cause mortality within the younger (<70 years of age) group from lag days 0 to 2 with the strongest effect detected on lag day 0 (IRR: 1.05; 95% CI: 1.01, 1.10) whereas in the older (70+ years of age) group, heat wave effects were only seen on lag day 0 (IRR: 1.03; 95% CI: 1.01, 1.06) (Figure 3). Cold wave–associated mortality risks were observed in the younger age group from lag day 2 to 6 with the highest risk at lag days 3 and 4 (IRR lag day 3: 1.05; 95% CI: 1.00, 1.09). In the older age group, cold wave–related effects persisted from lag day 3 to 5 and lag day 7 with the highest risk at lag day 4 (IRR: 1.04; 95% CI: 1.02, 1.07) (Figure 3). Age group estimates for heat and cold waves were not statistically different from each other (Table S4).

Gender. Cisgender men had heat wave–related mortality risk at lag day 0 (IRR: 1.03; 95% CI: 1.01, 1.06), whereas cisgender women had heat wave–associated mortality risk from lag days 0 to 2 with the greatest estimated risk on lag day 1 (IRR: 1.26; 95% CI: 1.10, 1.44), a 25% significant difference in risk compared to cisgender men on that same day (Figure 4; Table S5). For cold waves, cisgender men had an elevated risk of mortality at all lag days 2 to 7 with the greatest risk seen on lag day 4 (IRR: 1.04; 95% CI: 1.02, 1.07). The point estimates for cold wave–related mortality among cisgender women were similar to cisgender men; however, the estimates were less statistically precise (Figure 4). A small number of individuals identified as transgender ($n = 6$) and were excluded.

Table 2. Frequencies of heat and cold wave exposure for deceased veterans with COPD (2016 to 2021, $n = 377{,}545$) in the VHA health care system stratified by mortality (event) and referent day status.

	Warm season			Cold season		
Category	Heat wave	Non–heat wave	Total	Cold wave	Non–cold wave	Total
Exposed veterans [n (%)][a]	52,258 (28.4%)	131,467 (71.6%)	183,725	47,802 (24.7%)	146,018 (75.3%)	193,820
Exposure during event day [days (%)][b]	17,621 (9.6%)	166,104 (90.4%)	183,725	13,961 (7.2%)	179,859 (92.8%)	193,820
Exposure during referent day [days (%)][c]	58,246 (9.3%)	568,087 (90.7%)	626,333	46,355 (7.1%)	610,286 (92.9%)	656,641
Total study days (%)[d]	75,867 (9.4%)	734,191 (90.6%)	810,058	60,316 (7.1%)	790,145 (92.9%)	850,461

Note: Heat waves defined as 2+ consecutive days where the ambient mean daily temperature exceeded the 90th percentile of ambient mean temperature values for the warm season (April to September) from 1992 to 2021. Cold waves defined as 2+ consecutive days where the ambient mean daily temperature was below the 10th percentile of ambient mean temperature values for the cold season (October to March) from 1992 to 2021. COPD, chronic obstructive pulmonary disease; VHA, Veterans Health Administration.
[a]Where veterans who were exposed on either an event or referent day were considered as exposed. This row represents counts of unique deceased veterans who died during the warm or cold season.
[b]Counts only include exposure during the event day (lag day 0) for each deceased veteran.
[c]The unit of measurement for this row is days as veterans have multiple matched referent days.
[d]Where the total number of event and referent days used for the study were included in the totals for this row.

Table 3. Meteorological and air pollution data summaries on days of mortality for veterans with COPD (2016 to 2021) in the VHA health care system stratified by heat and cold wave status.

Exposure (mean ± SD)	Heat wave	Non–heat wave	Cold wave	Non–cold wave
Mean temperature (°C)	27.91 ± 3.07	20.49 ± 6.41	-4.55 ± 8.64	9.01 ± 8.18
Total precipitation (mm)	2.27 ± 6.90	3.66 ± 10.19	1.25 ± 4.45	2.86 ± 8.21
Mean specific humidity (g/kg)	14.1 ± 3.97	10.5 ± 4.41	2.27 ± 1.72	5.33 ± 3.24
Mean wind speed (m/s)	3.39 ± 1.34	3.75 ± 1.54	4.69 ± 2.09	4.27 ± 1.86
Mean $PM_{2.5}$ (μ/m^3)[a]	9.75 ± 4.39	7.66 ± 3.62	8.55 ± 3.94	8.38 ± 4.14

Note: Heat waves defined as 2+ consecutive days where the ambient mean daily temperature exceeded the 90th percentile of ambient mean temperature values for the warm season (April to September) from 1992 to 2021. Cold waves defined as 2+ consecutive days where the ambient mean daily temperature was below the 10th percentile of ambient mean temperature values for the cold season (October to March) from 1992 to 2021. COPD, chronic obstructive pulmonary disease; SD, standard deviation; VHA, Veterans Health Administration.

[a]$PM_{2.5}$ data was assigned only to a subset population of veterans who lived within a 10-km buffer of a valid air monitor ($n = 20,735$ warm season, $n = 21,535$ cold season). An average daily value of all $PM_{2.5}$ monitors within a 10-km buffer for each of the geocoded home location of these Veterans was calculated.

Race. Black patients had the largest overall risk of heat wave–associated mortality among all race groups with the greatest risk on lag day 0 (IRR: 1.09; 95% CI: 1.02, 1.15). White patients also showed heightened but smaller heat wave mortality associations on lag day 0 (Figure 5) while all other race groups, including patients with missing race data, showed no associations with heat waves (Table S6). AIAN patients had relatively large cold wave–related mortality risks on lag days 3 to 5 with the greatest effect seen on lag day 4 (IRR: 1.32; 95% CI: 1.08, 1.62). Among white patients, cold wave associations with mortality were not detected until lag day 3 with gradually increasing risk that plateaued at lag day 4 (IRR: 1.04; 95% CI: 1.02, 1.07) with lower but heightened risks through lag day 6 (Figure 5). AAPI and black patients' point estimates for cold wave–related mortality risk followed a similar trend to white patients; however, the estimates were less statistically precise driven in part by a smaller sample size compared to white patients (Table S6). Patients with missing race data had relatively large cold wave–associated mortality risks throughout the entire 7-d lag period, which peaked at lag day 7 (IRR: 1.09; 95% CI: 1.01, 1.17).

Ethnicity. Heat wave effects among non-Hispanic patients lasted from lag days 0 to 1 with the strongest effect on lag day 0 (IRR: 1.04; 95% CI: 1.02, 1.06). Hispanic patients did not have any associations with heat waves (Table S7). For cold waves, non-Hispanic patients had associations from lag days 2 to 6 with lag day 4 having the greatest risk of all-cause mortality (IRR: 1.04; 95% CI: 1.02, 1.07). Hispanic patients showed much larger cold wave–associated risk from lag days 4 to 5 with the greatest risk seen on lag day 4 (IRR: 1.15; 95% CI: 1.00, 1.32), but we did not observe significant differences in heat and cold wave effects by ethnicity (Table S7). Individuals with missing ethnicity data comprised 4.1% of veterans and were not evaluated as a separate stratum.

Sensitivity Analyses

Our sensitivity analysis for more stringent percentile thresholds of heat and cold waves illustrated a trend of robustness in our interpretation, although higher percentiles of heat waves did elicit an elevated risk of mortality on lag day 0 (Table S8). Cold wave results were generally unchanged, except for the first percentile of exposure, which showed an increased risk of mortality on lag day 6 (Table S8). More stringent percentile thresholds for both heat and cold waves resulted in a substantial decrease in exposed mortality days, which limits our ability to evaluate broader trends and distinctions within at-risk subpopulations.

Changing the reference period from a 30-year to a 20-year period for heat and cold waves did not impact our results (Table S9). Our model results were also robust to the exclusion of patients who were exposed to long duration heat and cold wave events and to the

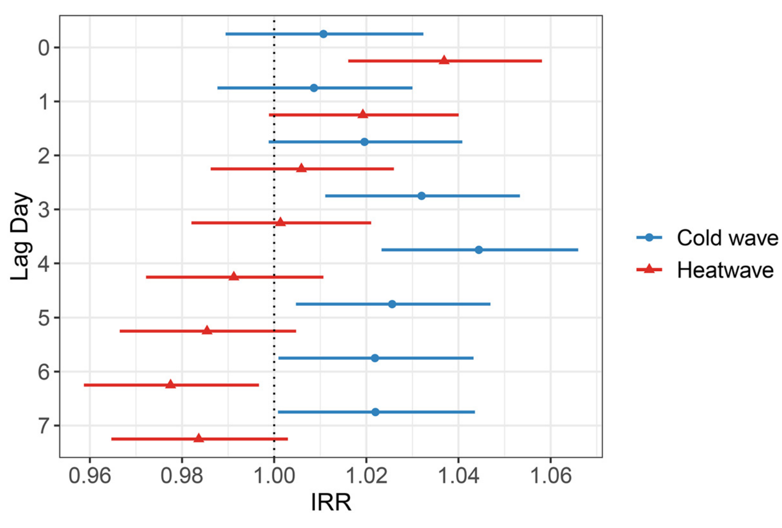

Figure 2. The estimated incidence rate ratio (IRR) for heat and cold wave associations with all-cause mortality among veterans with COPD (2016 to 2021, $n = 377,545$) from lag day 0 to 7. Heat waves defined as 2+ consecutive days where the ambient mean daily temperature exceeded the 90th percentile of ambient mean temperature values for the warm season (April to September) from 1992 to 2021. Cold waves defined as 2+ consecutive days where the ambient mean daily temperature was below the 10th percentile of ambient mean temperature values for the cold season (October to March) from 1992 to 2021. Estimates (95% CIs) were generated via conditional logistic regression models adjusted for daily total precipitation, mean wind speed, mean specific humidity, and holiday status. Points represent the estimated IRR and lines denote the 95% CI of the estimated IRR. Numeric data can be found in Table S3. Note: CI, confidence interval; COPD, chronic obstructive pulmonary disease.

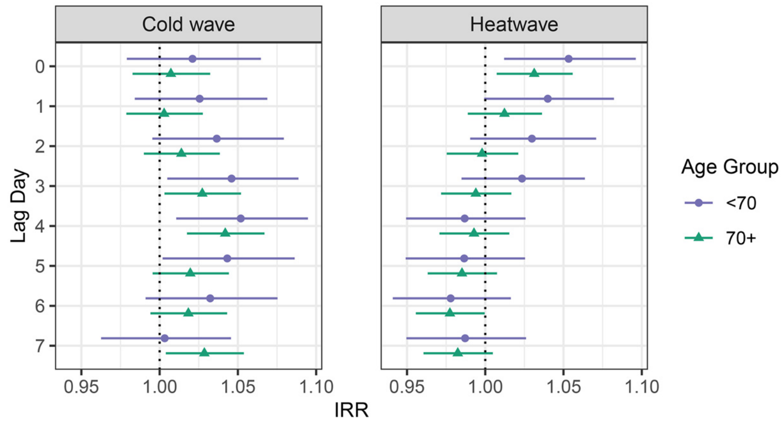

Figure 3. The estimated incidence rate ratio (IRR) for heat and cold wave associations with all-cause mortality among veterans with COPD (2016 to 2021, $n = 377{,}545$) from lag day 0 to 7, stratified by age group. Heat waves defined as 2+ consecutive days where the ambient mean daily temperature exceeded the 90th percentile of ambient mean temperature values for the warm season (April to September) from 1992 to 2021. Cold waves defined as 2+ consecutive days where the ambient mean daily temperature was below the 10th percentile of ambient mean temperature values for the cold season (October to March) from 1992 to 2021. Estimates (95% CIs) were generated via conditional logistic regression models adjusted for daily total precipitation, mean wind speed, mean specific humidity, and holiday status. Points represent the estimated IRR and lines denote the 95% CI of the estimated IRR. Numeric data can be found in Table S4. Note: CI, confidence interval; COPD, chronic obstructive pulmonary disease.

exclusion of patients who resided in locales with mild 30-year percentile threshold values (Tables S10 to S11).

In our assessment evaluating confounding bias by air pollution ($PM_{2.5}$), we found minimal changes to the effect estimate for heat waves (Table S12). When adjusting for daily mean $PM_{2.5}$ among patients who lived within 10 km of an EPA air monitor, the IRR at lag day 0 was 1.12 (95% CI: 1.05, 1.18) compared to 1.11 (95% CI: 1.05, 1.18) in a model without daily mean $PM_{2.5}$. For cold waves, estimates were unchanged in models with and without daily mean $PM_{2.5}$ adjustment (Table S12).

In the sensitivity assessment evaluating potential COVID-19 pandemic influences, we identified significant differences in heat and cold wave mortality associations for patients who died pre vs. post the COVID-19 emergency declaration (Table S13). To assess whether this difference was attributable to COVID-19 incidence, we ran new models including state-level weekly COVID-19 case rates per 100,000 as a fixed effect into statistical models. No changes were observed in the heat and cold wave effect estimates, suggesting that any lag-specific differences in heat and cold wave associations were not attributable to underlying incidence of COVID-19 cases (Table S14).

Discussion

Our findings demonstrate an increased risk of mortality associated with heat and cold waves among a population of veterans diagnosed with COPD. Heat waves had an immediate impact on all-cause mortality, showing the greatest mortality risk on lag day 0 for all populations except cisgender women. The finding of acute, intense heat wave effects is a common observation in other studies.[33,34] Conversely, cold wave effects demonstrated a delayed response starting on lag day 2, with the greatest effect detected at lag day 4 for most populations, although elevated risk persisted throughout the remainder of the 7-d exposure period. Within specific subpopulations, the effect of heat waves was larger in women than in men and in black veterans than in white veterans. Of note, the effect of cold waves was greater in AIAN and Hispanic veterans compared to white and non-Hispanic veterans, respectively.

A potential explanation for the disparate responses in heat and cold wave effects may be attributed to the underlying cause of death. Heat waves are predominately associated with more acute causes of death such as cardiovascular dysfunction or heat stress.[35,36] Cardiovascular-related mortality events are the primary cause of death attributable to extreme heat.[37] As the body

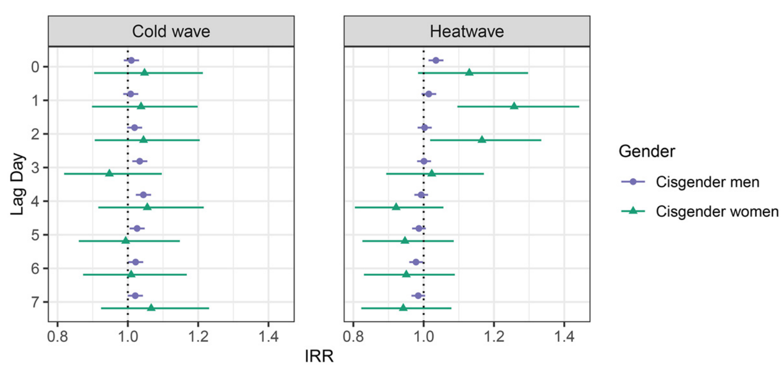

Figure 4. The estimated incidence rate ratio (IRR) for heat and cold wave associations with all-cause mortality among veterans with COPD (2016 to 2021, $n = 377{,}545$) from lag day 0 to 7, stratified by self-reported gender. Heat waves defined as 2+ consecutive days where the ambient mean daily temperature exceeded the 90th percentile of ambient mean temperature values for the warm season (April to September) from 1992 to 2021. Cold waves defined as 2+ consecutive days where the ambient mean daily temperature was below the 10th percentile of ambient mean temperature values for the cold season (October to March) from 1992 to 2021. Estimates (95% CIs) were generated via conditional logistic regression models adjusted for daily total precipitation, mean wind speed, mean specific humidity, and holiday status. Points represent the estimated IRR and lines denote the 95% CI of the estimated IRR. Numeric data can be found in Table S5. Note: CI, confidence interval; COPD, chronic obstructive pulmonary disease.

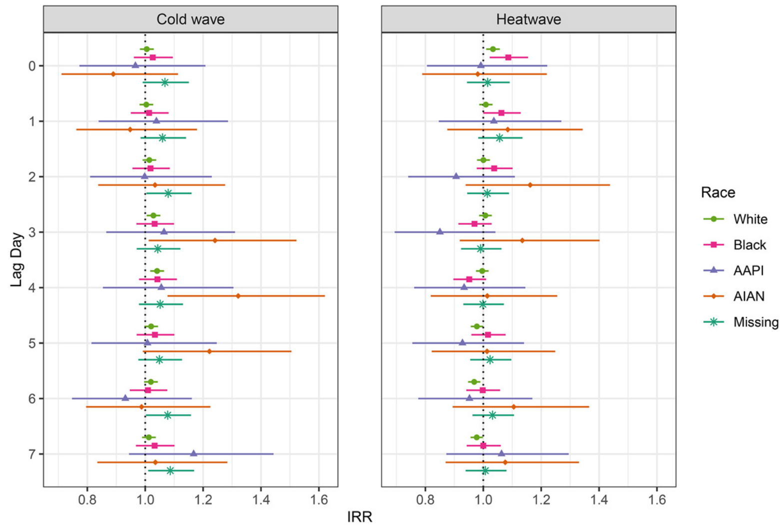

Figure 5. The estimated incidence rate ratio (IRR) for heat and cold wave associations with all-cause mortality among veterans with COPD (2016 to 2021, $n = 377{,}545$) from lag day 0 to 7, stratified by self-reported race. Heat waves defined as 2+ consecutive days where the ambient mean daily temperature exceeded the 90th percentile of ambient mean temperature values for the warm season (April to September) from 1992 to 2021. Cold waves defined as 2+ consecutive days where the ambient mean daily temperature was below the 10th percentile of ambient mean temperature values for the cold season (October to March) from 1992 to 2021. Estimates (95% CIs) were generated via conditional logistic regression models adjusted for daily total precipitation, mean wind speed, mean specific humidity, and holiday status. Points represent the estimated IRR and lines denote the 95% CI of the estimated IRR. Numeric data can be found in Table S6. Note: CI, confidence interval; COPD, chronic obstructive pulmonary disease.

attempts to thermoregulate via vasodilation, there can be a mismatch between increased cardiac demand and the ability of the heart to pump blood faster to meet this demand especially among individuals with underlying cardiac impairments.[37] This mismatch can cascade into severe cardiovascular health events including cardiovascular collapse.[37] There may also be a direct impact of extreme heat on the respiratory system although it has yet to be known how extreme heat impacts COPD.[38] Among individuals with asthma, research suggested inhalation of hot and humid air may induce bronchoconstriction mediated via the cholinergic reflex.[39]

The biological mechanisms underlying delayed effects of cold waves on health risks are less understood and may be most associated with more subacute causes of death such as COPD exacerbations.[40] In a population of individuals with COPD, delayed impacts of cold wave–associated mortality may be attributed to viral respiratory infections[41–43] and bacterial pneumonia,[41,42] both more common in the cold season of the year.[41–43] Higher rates of adverse COPD-related outcomes, including exacerbations and hospitalizations, in the cold season is another well-documented phenomenon that may explain our results.[44–46] Inflammation and bronchoconstriction are two postulated mechanisms by which cold exposure negatively affects individuals with COPD.[38,41]

Both heat waves and cold waves conferred a similar absolute risk of mortality on their strongest lag days in the veteran population with 651 deaths per 100,000 attributable to heat wave lag day 0 exposure and 687 deaths per 100,000 attributable to cold wave lag day 4 exposure, respectively. Cold waves had a higher AR due to the elevated mortality rates in the cold season compared to the warm season. These attributable risk measures are effective in illustrating the public health impact of extreme weather exposure among this vulnerable population and may be useful to both physicians and patients in assessing the potential benefits of engaging in protective behaviors during periods of extremely hot or cold weather and improving the housing conditions of individuals living with COPD.

Our results for heat and cold wave mortality risks on the multiplicative scale were similar to those reported in other studies of the general population. The increase in heat wave–associated risk for mortality in the general population ranged from 3% to 24.6%[19,20,36,47–51] compared to our highest estimated mortality risk of 4%. Cold wave–associated risk for mortality in the general population ranged from a relative risk (RR) of 1.01 to 1.57.[52–56] A recent meta-analysis reported an RR of 1.10 (95% CI: 1.04 to 1.07)[57] for cold wave effects on all-cause mortality compared with our highest estimated IRR of 1.04. While our estimated multiplicative associations for heat and cold waves were relatively lower than most estimates reported in the literature, they fall within the range of previously reported effect estimates. The cause of this attenuation is unknown but may be attributed to our population being composed entirely of individuals diagnosed with a chronic respiratory disease. Such individuals, while more susceptible, may also be more conscious of their fragile health state and take precautionary measures to avoid extreme weather exposure compared to a healthy population that may be outdoors in suboptimal temperatures. One study detected a 4.9% decrease in asthma hospitalizations during cold wave days, which the authors suggested could be related to individuals with asthma taking extra medical precautions during extremely cold weather events.[58]

Prior research provides evidence for sex-based disparities with higher heat wave–related mortality risk in women than men, attributed to differences in physiology, behavioral patterns, and occuptation.[3,48] Our results were congruent with the prior literature in that cisgender women had a significantly greater heat wave–associated mortality risk than cisgender men. Heat wave effects on mortality for men ranged from RR 1.02 to 1.06[19,20,51] and for women from RR 1.06 to 1.12[19,20,51] compared to our maximum effect estimates of IRR 1.03 in cisgender men and IRR 1.26 in cisgender women. Our results may suggest cisgender women veterans with COPD have greater heat wave–related mortality risk compared to previous studies in the general population. While our point estimates for cold wave–related mortality among cisgender women followed a similar trend as cisgender men, the estimates were imprecise and did not indicate an association unlike prior research.[53,56]

Age stratified estimates failed to detect differences between older and younger veterans in our population contrary to other research that found age–related disparities in heat[19,20,34,47,51] and cold wave–associated mortality.[22,52,54,55,57] Indeed, a recent review concluded strong evidence for higher mortality risk in older populations due to extreme heat and cold exposure attributed to physiology, behavioral practices, prevalence of comorbidities, living alone, and access to indoor heat and air conditioning.[3] Furthermore, it would be hypothesized that as a veteran aged and transitioned into a retirement phase, living conditions, behaviors, and physical health would change, which could enhance susceptibility to extreme weather events, but this has not been formally tested. The lack of disparate mortality risk between the age groups in our study could, however, be reflective of the quality and access of care received at the VHA.

Our results mostly failed to show differences in the effects of heat and cold waves when comparing racial and ethnic minorities to white and non-Hispanic individuals. This may be due to the relatively small number of veterans in our cohort who identified as racial and ethnic minorities combined with a scarcity of mortality events occurring on heat and cold wave exposure days. Some of our effect estimates indicated heightened heat wave–related mortality risk particularly for black veterans and cold wave–related mortality risk for AIAN and Hispanic veterans, although caution should be used in interpreting AIAN mortality risks as sample sizes in this group were relatively small. Another plausible explanation for the lack of race and ethnicity-based differences is that the VHA health care system has fewer access barriers compared to private health care for veterans. Indeed, the VHA provides a high level of care often matching or outperforming care at peer non-VHA health care facilities.[59,60] In treatment of COPD specifically, the VHA outperforms 94% of health care market regions compared to non-VHA hospitals.[60] As an equal access health care system with facilities that are widespread, including many clinics in rural areas, this may minimize racial inequities in care within the VHA. One study estimated the 30-d mortality rate in patients sent by ambulance to a VHA hospital was 20.1% lower[59] compared to non-VHA hospitals with even better outcomes for black and Hispanic patients with a 25.8%[59] and 22.7%[59] lower mortality rate, respectively. This is not to say that there are no racial disparities in health outcomes within the VHA, only that these disparities may be smaller than in the nonveteran population. One study comparing mortality in white vs. black veterans compared to nonveterans found the disparity in mortality rates to be smaller in the veteran population than the nonveteran population, which may be due to the relatively elevated socioeconomic status of black veterans compared to black nonveterans.[61]

Our work has several limitations. The composition of the study cohort was overwhelmingly male and older, the latter reflecting that COPD is predominantly a disease of older adults. There was missingness in the race data that could have hampered our ability to detect potential differences in heat and cold wave mortality risk. In addition, the specific causes of mortality could not be distinguished. We did not have data on the severity of COPD among our cohort, which prohibited an evaluation of heat and cold wave–associated mortality risks with respect to severity of disease. This is important to consider for future research as individuals with severe disease may have a larger risk of mortality associated with extreme weather exposure compared to those with mild disease. Exposure misclassification is possible, as we assigned heat and cold wave exposure to a geocoded residence which is a proxy for outdoor exposure and cannot account for routine or seasonal travel. It is also possible some veterans with COPD were missed in our study population due to misdiagnoses or if a veteran switched to private medical insurance. We were limited in using ICD codes alone to identify patients with COPD. Diagnostic spirometry information is considered a gold standard measure in identifying individuals with COPD, but we did not have spirometry information for our cohort and these data are not uniformly collected in the VHA Health Care System. One prior nationwide study of veterans found <52% had spirometry information within 2 years of the initial date of COPD diagnosis.[62] However, prior research in VHA populations found ICD codes perform modestly well with fairly high specificity and moderate sensitivity.[63–65] Lastly, our study was a relatively short 5-year time period that evaluated a rare exposure, which limits our ability to detect associations within subpopulations.

The primary strength of our study was the implementation of an individual-level national assessment focused entirely on individuals with a chronic respiratory disease, a growing population with high vulnerability to extreme weather events. The results of this study will inform clinical, policy, and public health practice on the effects of climate change and extreme weather events among individuals with chronic respiratory illnesses. Our study may also facilitate the development of targeted early warning systems for heat and cold waves among high-risk populations, as current warning systems are built primarily for the general population which may have a higher tolerance for perturbations in ambient temperature compared to high-risk groups.

Conclusion

In the United States veteran population with COPD, heat and cold waves increased the risk of all-cause mortality, with cold waves conferring a greater number of excess deaths compared to heat waves. Cisgender women were estimated to have greater risks of mortality due to heat wave exposure with suggestive evidence of elevated heat wave risk in black veterans. AIAN and Hispanic veterans may have elevated risk due to cold wave exposure. This study elucidated the impacts of heat and cold waves among a population of veterans with a chronic respiratory disease, and these results can inform future clinical treatment and public health policy to lessen the burden of climate-related hazards in high-risk populations.

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References

1. Bell JE, Brown CL, Conlon K, Herring S, Kunkel KE, Lawrimore J, et al. 2018. Changes in extreme events and the potential impacts on human health. J Air Waste Manag Assoc 68(4):265–287, PMID: 29186670, https://doi.org/10.1080/10962247.2017.1401017.
2. IPCC (Intergovernmental Panel on Climate Change). 2023. *Climate Change 2022: Impacts, Adaptation, and Vulnerability. Working Group II Contribution to the Sixth Assessment Report of the Intergovernmental Panel on Climate Change*. Cambridge UK: Cambridge University Press.
3. Son J-Y, Liu JC, Bell ML. 2019. Temperature-related mortality: a systematic review and investigation of effect modifiers. Environ Res Lett 14(7):073004, https://doi.org/10.1088/1748-9326/ab1cdb.
4. GOLD. 2020. *Global Initiative for Chronic Obstructive Lung Disease*. https://goldcopd.org/wp-content/uploads/2019/11/GOLD-Pocket-Guide-2020-final-wms.pdf [accessed 23 March 2023].
5. Wheaton AG, Liu Y, Croft JB, VanFrank B, Croxton TL, Punturieri A, et al. 2019. Chronic obstructive pulmonary disease and smoking status—United States, 2017. Mmwr Morb Mortal Wkly Rep 68(24):533–538, PMID: 31220055, https://doi.org/10.15585/mmwr.mm6824a1.
6. Zarrabian B, Mirsaeidi M. 2021. A trend analysis of chronic obstructive pulmonary disease mortality in the United States by race and sex. Ann Am Thorac Soc 18(7):1138–1146, PMID: 33347376, https://doi.org/10.1513/AnnalsATS.202007-822OC.
7. Carlson SA, Wheaton AG, Watson KB, Liu Y, Croft JB, Greenlund KJ. 2022. Geographic differences in sex-specific chronic obstructive pulmonary disease mortality rate trends among adults aged ≥25 years—United States, 1999–2019. Mmwr Morb Mortal Wkly Rep 71(18):613–618, PMID: 35511711, https://doi.org/10.15585/mmwr.mm7118a1.
8. Rabe KF, Watz H. 2017. Chronic obstructive pulmonary disease. Lancet 389(10082):1931–1940, PMID: 28513453, https://doi.org/10.1016/S0140-6736(17)31222-9.
9. Smith M, Wrobel J. 2014. Epidemiology and clinical impact of major comorbidities in patients with COPD. Int J Chron Obstruct Pulmon Dis 9:871–888, PMID: 25210449, https://doi.org/10.2147/COPD.S49621.
10. Anderson BG, Bell ML. 2009. Weather-related mortality: how heat, cold, and heat waves affect mortality in the United States. Epidemiology 20(2):205–213, PMID: 19194300, https://doi.org/10.1097/EDE.0b013e318190ee08.
11. Gasparrini A, Guo Y, Hashizume M, Lavigne E, Zanobetti A, Schwartz J, et al. 2015. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. Lancet 386(9991):369–375, PMID: 26003380, https://doi.org/10.1016/S0140-6736(14)62114-0.
12. Zhao Q, Guo Y, Ye T, Gasparrini A, Tong S, Overcenco A, et al. 2021. Global, regional, and national burden of mortality associated with non-optimal ambient temperatures from 2000 to 2019: a three-stage modelling study. Lancet Planetary Health 5(7):e415–e425, https://doi.org/10.1016/S2542-5196(21)00081-4.
13. Lumley T, Levy D. 2000. Bias in the case-crossover design: implications for studies of air pollution. Environmetrics 11(6):689–704, https://doi.org/10.1002/1099-095X(200011/12)11:6<689::AID-ENV439>3.0.CO;2-N.
14. Maclure M. 1991. The case-crossover design: a method for studying transient effects on the risk of acute events. Am J Epidemiol 133(2):144–153, PMID: 1985444, https://doi.org/10.1093/oxfordjournals.aje.a115853.
15. U.S. Department of Veterans Affairs. 2019. *Determining Veteran Status*. https://www.va.gov/OSDBU/docs/Determining-Veteran-Status.pdf [accessed 12 March 2022].
16. Gothe H, Rajsic S, Vukicevic D, Schoenfelder T, Jahn B, Geiger-Gritsch S, et al. 2019. Algorithms to identify COPD in health systems with and without access to ICD coding: a systematic review. BMC Health Serv Res 19(1):737, PMID: 31640678, https://doi.org/10.1186/s12913-019-4574-3.
17. United States Department of Veterans Affairs Information Resource Center. 2016. *VIReC Research User Guide: PSSG Geocoded Enrollee Files, 2015 Edition*. Washington DC: US Department of Veterans Affairs.
18. Abatzoglou JT. 2013. Development of gridded surface meteorological data for ecological applications and modelling. Intl Journal of Climatology 33(1):121–131, https://doi.org/10.1002/joc.3413.
19. Kollanus V, Tiittanen P, Lanki T. 2021. Mortality risk related to heatwaves in Finland – factors affecting vulnerability. Environ Res 201:111503, PMID: 34144011, https://doi.org/10.1016/j.envres.2021.111503.
20. Wang XY, Guo Y, FitzGerald G, Aitken P, Tippett V, Chen D, et al. 2015. The impacts of heatwaves on mortality differ with different study periods: a multicity time series investigation. PLoS One 10(7):e0134233, PMID: 26217945, https://doi.org/10.1371/journal.pone.0134233.
21. Gao J, Yu F, Xu Z, Duan J, Cheng Q, Bai L, et al. 2019. The association between cold spells and admissions of ischemic stroke in Hefei, China: modified by gender and age. Sci Total Environ 669:140–147, PMID: 30878922, https://doi.org/10.1016/j.scitotenv.2019.02.452.
22. Liu Y, Chen Y, Kong D, Liu X, Fu J, Zhang Y, et al. 2021. Short-term effects of cold spells on hospitalisations for acute exacerbation of chronic obstructive pulmonary disease: a time-series study in Beijing, China. BMJ Open 11(1):e039745, https://doi.org/10.1136/bmjopen-2020-039745.
23. Cheng Q, Wang X, Wei Q, Bai L, Zhang Y, Gao J, et al. 2019. The short-term effects of cold spells on pediatric outpatient admission for allergic rhinitis in Hefei, China. Sci Total Environ 664:374–380, PMID: 30743130, https://doi.org/10.1016/j.scitotenv.2019.01.237.
24. US EPA. 2013. *Air Quality System (AQS)*. https://aqs.epa.gov/aqsweb/airdata/download_files.html#Daily [accessed 28 November 2022].
25. Janes H, Sheppard L, Lumley T. 2005. Case–crossover analyses of air pollution exposure data: referent selection strategies and their implications for bias. Epidemiology 16(6):717–726, PMID: 16222160, https://doi.org/10.1097/01.ede.0000181315.18836.9d.
26. Mittleman MA, Mostofsky E. 2014. Exchangeability in the case-crossover design. Int J Epidemiol 43(5):1645–1655, PMID: 24756878, https://doi.org/10.1093/ije/dyu081.
27. Davis RE, McGregor GR, Enfield KB. 2016. Humidity: a review and primer on atmospheric moisture and human health. Environ Res 144(pt A):106–116, PMID: 26599589, https://doi.org/10.1016/j.envres.2015.10.014.
28. U.S. Office of Personnel Management. 2024. *Holidays Work Schedules and Pay*. Washington DC: U.S. Office of Personnel Management. https://www.opm.gov/policy-data-oversight/pay-leave/pay-administration/fact-sheets/holidays-work-schedules-and-pay/ [accessed 12 February 2023].
29. Lu Y, Zeger SL. 2007. On the equivalence of case-crossover and time series methods in environmental epidemiology. Biostatistics 8(2):337–344, PMID: 16809430, https://doi.org/10.1093/biostatistics/kxl013.
30. Altman DG, Bland JM. 2003. Statistics notes: interaction revisited: the difference between two estimates. BMJ 326(7382):219, PMID: 12543843, https://doi.org/10.1136/bmj.326.7382.219.
31. CDC (Centers for Disease Control and Prevention). 2023. *CDC Museum COVID-19 Timeline*. Atlanta, GA: Centers for Disease Control and Prevention. https://www.cdc.gov/museum/timeline/covid19.html [accessed 22 March 2023].
32. CDC (Centers for Disease Control and Prevention). 2023. *Provisional COVID-19 Death Counts by Week Ending Date and State*. Atlanta, GA: Centers for Disease Control and Prevention. https://data.cdc.gov/NCHS/Provisional-COVID-19-Death-Counts-by-Week-Ending-D/r8kw-7aab [accessed 23 March 2023].
33. Anderson GB, Dominici F, Wang Y, McCormack MC, Bell ML, Peng RD. 2013. Heat-related emergency hospitalizations for respiratory diseases in the Medicare population. Am J Respir Crit Care Med 187(10):1098–1103, PMID: 23491405, https://doi.org/10.1164/rccm.201211-1969OC.
34. Bobb JF, Obermeyer Z, Wang Y, Dominici F. 2014. Cause-specific risk of hospital admission related to extreme heat in older adults. JAMA 312(24):2659–2667, PMID: 25536257, https://doi.org/10.1001/jama.2014.15715.
35. Cheng J, Xu Z, Bambrick H, Prescott V, Wang N, Zhang Y, et al. 2019. Cardiorespiratory effects of heatwaves: a systematic review and meta-analysis of global epidemiological evidence. Environ Res 177:108610, PMID: 31376629, https://doi.org/10.1016/j.envres.2019.108610.
36. Xu Z, FitzGerald G, Guo Y, Jalaludin B, Tong S. 2016. Impact of heatwave on mortality under different heatwave definitions: a systematic review and meta-analysis. Environ Int 89–90:193–203, PMID: 26878285, https://doi.org/10.1016/j.envint.2016.02.007.
37. Ebi KL, Capon A, Berry P, Broderick C, de Dear R, Havenith G, et al. 2021. Hot weather and heat extremes: health risks. Lancet 398(10301):698–708, PMID: 34419205, https://doi.org/10.1016/S0140-6736(21)01208-3.
38. Hansel NN, McCormack MC, Kim V. 2016. The effects of air pollution and temperature on COPD. COPD 13(3):372–379, PMID: 26683097, https://doi.org/10.3109/15412555.2015.1089846.
39. Hayes D, Collins PB, Khosravi M, Lin R-L, Lee L-Y. 2012. Bronchoconstriction triggered by breathing hot humid air in patients with asthma: role of cholinergic reflex. Am J Respir Crit Care Med 185(11):1190–1196, PMID: 22505744, https://doi.org/10.1164/rccm.201201-0088OC.
40. Tseng C-M, Chen Y-T, Ou S-M, Hsiao Y-H, Li S-Y, Wang S-J, et al. 2013. The effect of cold temperature on increased exacerbation of chronic obstructive pulmonary disease: a nationwide study. PLoS One 8(3):e57066, PMID: 23554858, https://doi.org/10.1371/journal.pone.0057066.
41. Gayle AV, Quint JK, Fuertes EL. 2021. Understanding the relationships between environmental factors and exacerbations of COPD. Expert Rev Respir Med 15(1):39–50, PMID: 32713218, https://doi.org/10.1080/17476348.2020.1801426.
42. Hicks A, Healy E, Sandeman N, Feelisch M, Wilkinson T. 2018. A time for everything and everything in its time—exploring the mechanisms underlying seasonality of COPD exacerbations. Int J Chron Obstruct Pulmon Dis 13:2739–2749, PMID: 30233164, https://doi.org/10.2147/COPD.S146015.
43. Javorac J, Jevtić M, Živanović D, Ilić M, Bijelović S, Dragić N. 2021. What are the effects of meteorological factors on exacerbations of chronic obstructive pulmonary disease? Atmosphere 12(4):442, https://doi.org/10.3390/atmos12040442.
44. Donaldson GC, Wedzicha JA. 2014. The causes and consequences of seasonal variation in COPD exacerbations. Int J Chron Obstruct Pulmon Dis 9:1101–1110, PMID: 25336941, https://doi.org/10.2147/COPD.S54475.

45. Jenkins CR, Celli B, Anderson JA, Ferguson GT, Jones PW, Vestbo J, et al. 2012. Seasonality and determinants of moderate and severe COPD exacerbations in the TORCH study. Eur Respir J 39(1):38–45, PMID: 21737561, https://doi.org/10.1183/09031936.00194610.
46. Rabe KF, Fabbri LM, Vogelmeier C, Kögler H, Schmidt H, Beeh KM, et al. 2013. Seasonal distribution of COPD exacerbations in the prevention of exacerbations with tiotropium in COPD trial. Chest 143(3):711–719, PMID: 23188489, https://doi.org/10.1378/chest.12-1277.
47. Anderson GB, Bell ML. 2011. Heat waves in the United States: mortality risk during heat waves and effect modification by heat wave characteristics in 43 U.S. communities. Environ Health Perspect 119(2):210–218, PMID: 21084239, https://doi.org/10.1289/ehp.1002313.
48. Chen K, Bi J, Chen J, Chen X, Huang L, Zhou L. 2015. Influence of heat wave definitions to the added effect of heat waves on daily mortality in Nanjing, China. Sci Total Environ 506–507:18–25, PMID: 25460935, https://doi.org/10.1016/j.scitotenv.2014.10.092.
49. Kang C, Park C, Lee W, Pehlivan N, Choi M, Jang J, et al. 2020. Heatwave-related mortality risk and the risk-based definition of heat wave in South Korea: a nationwide time-series study for 2011–2017. Int J Environ Res Public Health 17(16):5720, PMID: 32784700, https://doi.org/10.3390/ijerph17165720.
50. Tong S, Wang XY, Barnett AG. 2010. Assessment of heat-related health impacts in Brisbane, Australia: comparison of different heatwave definitions. PLoS One 5(8):e12155, PMID: 20730050, https://doi.org/10.1371/journal.pone.0012155.
51. Yang J, Yin P, Sun J, Wang B, Zhou M, Li M, et al. 2019. Heatwave and mortality in 31 major Chinese cities: definition, vulnerability and implications. Sci Total Environ 649:695–702, PMID: 30176480, https://doi.org/10.1016/j.scitotenv.2018.08.332.
52. Wang L, Liu T, Hu M, Zeng W, Zhang Y, Rutherford S, et al. 2016. The impact of cold spells on mortality and effect modification by cold spell characteristics. Sci Rep 6:38380, PMID: 27922084, https://doi.org/10.1038/srep38380.
53. Chen J, Yang J, Zhou M, Yin P, Wang B, Liu J, et al. 2019. Cold spell and mortality in 31 Chinese capital cities: definitions, vulnerability and implications. Environ Int 128:271–278, PMID: 31071590, https://doi.org/10.1016/j.envint.2019.04.049.
54. Chen J, Dong H, Yang J, Li L, Jin J, Yang Z, et al. 2021. The impact of cold spells on mortality from a wide spectrum of diseases in Guangzhou, China. Environ Res Lett 16(1):015009, https://doi.org/10.1088/1748-9326/abd26f.
55. Lei J, Chen R, Yin P, Meng X, Zhang L, Liu C, et al. 2022. Association between cold spells and mortality risk and burden: a nationwide study in China. Environ Health Perspect 130(2):27006, PMID: 35157500, https://doi.org/10.1289/EHP9284.
56. Han J, Liu S, Zhang J, Zhou L, Fang Q, Zhang J, et al. 2017. The impact of temperature extremes on mortality: a time-series study in Jinan, China. BMJ Open 7(4):e014741, PMID: 28465307, https://doi.org/10.1136/bmjopen-2016-014741.
57. Ryti NRI, Guo Y, Jaakkola JJK. 2016. Global association of cold spells and adverse health effects: a systematic review and meta-analysis. Environ Health Perspect 124(1):12–22, PMID: 25978526, https://doi.org/10.1289/ehp.1408104.
58. Fitzgerald EF, Pantea C, Lin S. 2014. Cold spells and the risk of hospitalization for asthma: New York, USA 1991–2006. Lung 192(6):947–954, PMID: 25304443, https://doi.org/10.1007/s00408-014-9645-y.
59. Chan DC, Danesh K, Costantini S, Card D, Taylor L, Studdert DM. 2022. Mortality among US veterans after emergency visits to veterans affairs and other hospitals: retrospective cohort study. BMJ 376:e068099, PMID: 35173019, https://doi.org/10.1136/bmj-2021-068099.
60. Weeks WB, West AN. 2019. Veterans health administration hospitals outperform non–veterans health administration hospitals in most health care markets. Ann Intern Med 170(6):426–428, PMID: 30535282, https://doi.org/10.7326/M18-1540.
61. Sheehan C, Hayward MD. 2019. Black/white differences in mortality among veteran and non-veteran males. Soc Sci Res 79:101–114, PMID: 30857656, https://doi.org/10.1016/j.ssresearch.2019.02.006.
62. Baldomero AK, Kunisaki KM, Wendt CH, Bangerter A, Diem SJ, Ensrud KE, et al. 2022. Drive time and receipt of guideline-recommended screening, diagnosis, and treatment. JAMA Netw Open 5(11):e2240290, PMID: 36331503, https://doi.org/10.1001/jamanetworkopen.2022.40290.
63. Cooke CR, Joo MJ, Anderson SM, Lee TA, Udris EM, Johnson E, et al. 2011. The validity of using ICD-9 codes and pharmacy records to identify patients with chronic obstructive pulmonary disease. BMC Health Serv Res 11(1):37, PMID: 21324188, https://doi.org/10.1186/1472-6963-11-37.
64. Crothers K, Rodriguez C, Nance RM, Akgun K, Shahrir S, Kim J, et al. 2019. Accuracy of electronic health record data for the diagnosis of chronic obstructive pulmonary disease in persons living with HIV and uninfected persons. Pharmacoepidemiol Drug Saf 28(2):140–147, PMID: 29923258, https://doi.org/10.1002/pds.4567.
65. Justice AC, Lasky E, McGinnis KA, Skanderson M, Conigliaro J, Fultz SL, et al. 2006. Medical disease and alcohol use among veterans with human immunodeficiency infection: a comparison of disease measurement strategies. Med Care 44(8 Suppl 2):S52–S60, PMID: 16849969, https://doi.org/10.1097/01.mlr.0000228003.08925.8c.